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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,187	10/21/2005	Mark E Duggan	21368YP	1879

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EXAMINER	
ROBINSON, BINTA M	
ART UNIT	**PAPER NUMBER**
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,187	DUGGAN ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-4 and 6* is/are allowed.

6)☒ Claim(s) *5 and 7-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Claims 1-4, 6 are allowable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 5, line 1, page 51, the term "TFA" is unclear because it is an acronym and its meaning is unclear. What does this acronym stand for? It needs to be spelled out.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating some angiogenesis related cancers, allergy/asthma and hyperinsulinism, does not reasonably provide enablement for treating all cancers, all non-malignant diseases in which angiogenesis is implicated, all types of inflammation, autoimmune diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,

3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the treatment of cancer, non-malignant diseases, hyperproliferative disorders selected from inflammation, autoimmune diseases and allergy/asthma with the compounds of formula (I) as found in claim 1.

The state of the prior art

It is known in the state of the art that Ak1 controls a plethora of cellular responses and that the three Akt isoforms Akt1, Akt2, and Akt3 are ubiquitously expressed in all cell types and tissues. See page 3963 of Toker et. al. In normal and cancer cells, Akt regulates both growth and survival mechanisms and does so by phosphorylating a large number of substrates. See page 3963, column 1 of Toker et. al.

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. For example, evidence continues to accumulate that different isoforms of Akt have different functions in cells. See Toker et al. , page 3963. Ak1 and Ak2 knockout mice show distinct phenotypes with Ak1 null mice exhibiting growth defects, and Akt2 null mice exhibiting mainly defects in glucose homeostasis, these differences have yet to be correlated to differences at the isoforms. See page 3965, column 2 of Toker et. al. It may be true that AKT as an inhibitor of invasive migration may hold true only on a subset of tissues. See column 2, page 3965 of Toker et. al. Evidence continues to accumulate that different isoforms of Akt have different functions in cells, including in settings of human neoplasia. See page 3965, column 2 of Toker et. al. Some studies have revealed the expression of activated

Akt1, activated either as a myristolated membrane-bound form or a phosphorylation site mutant, potently blocked the in vitro migration and invasion of three distinct breast cancer cell lines. See column 2, page 3963 of Toker et. al.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of Akt-mediated diseases, whether the Akt was promoted or inhibited would affect the possible treatment of any disease.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compound of claim 1 and the inhibition of Akt, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of Akt, i.e. whether promotion or inhibition would be beneficial for the treatment of the diseases.
The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of claim 1 can inhibit the Akt which helps in the treatment of all cancers, all inflammation, hyperinsulinism. However, the specification is fails to provide guidance as to whether the diseases listed as Akt-mediated diseases, require the inhibition of Akt or the promotion of Akt for treatment, i.e. the specification fails to provide a correlation between the diseases listed and the inhibition of Akt.

The ***presence or absence of working examples***

The only direction or guidance present in the instant specification is found on page 46 of the specification regarding the in vivo inhibition of tumor growth in human cell lines, Heregulin stimulated Akt Activation assays on page 46 of the specification, cell based assays to determine the inhibition of Akt on page 46 of the specification, PKC assays on page 45 of the specification, PKA assay on page 44 of the specification and Akt Kinase assays on page 43 of the specification. Also, the compounds which are disclosed in the specification have no pharmacological data regarding the treatment of any disease and have no data on the possible treatment of Akt-mediated diseases that require the inhibition of Akt. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the inhibition of Akt.

The breadth of the claims

The breadth of the claims is the treatment of all cancers, all malignant tumors, allergy/asthma and hyperinsulinism, all non-malignant diseases in which angiogenesis is implicated, all types of inflammation, autoimmune diseases without regards as to the affect of Akt on the stated diseases.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification and when faced with

the unpredictability of the cancer therapy art in particular. The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the inhibition of Akt and would furthermore then have to determine whether the claimed compounds would provide treatment of the disease by the inhibition of Akt.

The level of the skill in the art

Even though the level of skill in the cancer therapy art is very high, based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims and lack of guidance and direction, one skilled in the art could not use the claimed invention without undue experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas McKenzie can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
October 13, 2006

THOMAS MCKENZIE, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600